

CLAIMS

1. A method of modulating NF- $\kappa$ B dependent gene expression in a cell said method comprised of modulating IKK $\alpha$  activity in the cell.

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2. The method of claim 1 wherein the expression of said NF- $\kappa$ B dependent gene is inhibited.

3. The method of claim 1 wherein IKK $\alpha$  activity is modulated by administration to a cell of siRNA directed to IKK $\alpha$ .

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4. The method of claim 3 wherein the transcription of said gene is modulated by administration of an siRNA selected from the list consisting of the compositions of SEQ. ID. NO. 2, SEQ. ID. NO. 3, SEQ. ID. NO. 4, SEQ. ID. NO. 5, SEQ. ID. NO 6 or SEQ. ID NO. 7.

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5. A method for selectively modulating expression of a gene whose expression is regulated by IKK $\alpha$ , the method comprising modulating IKK $\alpha$  activity such that expression of said gene is modulated.

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6. The method of claim 5, wherein the transcription of said gene is modulated by administration of an siRNA selected from the list consisting of the compositions of SEQ. ID NO. 2, SEQ. ID NO. 3, SEQ. ID NO. 4, SEQ. ID NO. 5, SEQ. ID NO. 6, or SEQ. ID NO. 7.

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7. The method of claim 5 wherein said gene is selected from the list consisting of IL-6, IL-8, Cox-2, ISG-15, IL-11, or GRO1.

8. The method of claim 5, wherein IKK $\alpha$  activity is modulated by administration of siRNA directed to IKK $\alpha$ .

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9. An siRNA composition comprised of siRNA sequence selected from the list consisting of SEQ. ID NO. 2, SEQ. ID NO. 3, SEQ. ID NO. 4, SEQ. ID NO. 5, SEQ. ID NO. 6, or SEQ. ID NO. 7.
- 5 10. An siRNA composition of claim 9 comprised of siRNA sequence of SEQ. ID NO. 2.
11. An siRNA composition of claim 9 comprised of siRNA sequence of SEQ. ID NO. 3.
- 10 12. An siRNA composition of claim 9 comprised of siRNA sequence of SEQ. ID NO. 4.
13. An siRNA composition of claim 9 comprised of siRNA sequence of SEQ. ID NO. 5.
- 15 14. An siRNA composition of claim 9 comprised of siRNA sequence of SEQ. ID NO. 6.
- 20 15. An siRNA composition of claim 9 comprised of siRNA sequence of SEQ. ID NO. 7.
16. A method for treating autoimmune and inflammatory disease in a mammal said method comprised of modulating the expression or activity of IKK $\alpha$ .
- 25 17. The method of claim 16 wherein the autoimmune and inflammatory disease is selected from the list consisting of asthma, SLE, rheumatoid arthritis, inflammatory bowel disease, and psoriasis.
- 30 18. The method of claim 16 wherein said disease is asthma.

19. The method of claim 16 wherein said disease is SLE.

20. The method of claim 16 wherein the IKK $\alpha$  activity is reduced by administering to a cell siRNA directed to IKK $\alpha$ .

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21. A method for identifying a compound for the treatment of autoimmune and inflammatory disease, said method comprised of the steps of:

a) incubating an IKK $\alpha$  protein in the presence of a potential inhibitor of IKK $\alpha$  activity;

10 b) measuring the loss of IKK $\alpha$  activity;

c) comparing the amount of IKK $\alpha$  activity present in the absence of a potential inhibitor.

22. The method of Claim 21 using a protein fragment of the IKK $\alpha$  protein.

15 23. The method of Claim 21 wherein the IKK $\alpha$  protein is substantially purified.

24. An siRNA compound 21-25 nucleotides in length that specifically hybridizes to a nucleic acid molecule encoding human IKK $\alpha$  of SEQ. ID. No. 1.

## SEQ. ID NO. 1

ATGGAGCGGCCCCCGGGGCTGCGGCCGGGCGCGGGCGGGCCCTGGGAGAT  
GCGGGAGCGGCTGGGCACCGGCGGCTTCGGGAACGTCTGTCTGTACCAGC  
5 ATCGGGAACCTTGATCTCAAAATAGCAATTAAGTCTTGTGCGCTAGAGCTA  
AGTACCAAAAACAGAGAACGATGGTGCCATGAAATCCAGATTATGAAGAA  
GTTGAACCATGCCAATGTTGTAAAGGCCTGTGATGTTCTCTGAAGAATTGA  
ATATTTTGATTTCATGATGTGCCTCTTCTAGCAATGGAATACTGTTCTGGA  
GGAGATCTCCGAAAGCTGCTCAACAAACCAGAAAATTGTTGTGGACTTAA  
10 AGAAAGCCAGATACTTTCTTTACTAAGTGATATAGGGTCTGGGATTCGAT  
ATTTGCATGAAAACAAAATTATACATCGAGATCTAAACCTGAAAACATA  
GTTCTTCAGGATGTTGGTGGAAGATAATACATAAAATAATTGATCTGGG  
ATATGCCAAAGATGTTGATCAAGGAAGTCTGTGTACATCTTTTGTGGGAA  
CACTGCAGTATCTGGCCCCAGAGCTCTTTGAGAATAAGCCTTACACAGCC  
15 ACTGTTGATTATTGGAGCTTTGGGACCATGGTATTTGAATGTATTGCTGG  
ATATAGGCCTTTTTTGCATCATCTGCAGCCATTTACCTGGCATGAGAAGA  
TTAAGAAGAAGGATCCAAAGTGTATATTGTCATGTGAAGAGATGTCAGGA  
GAAGTTCGGTTTTAGTAGCCATTTACCTCAACCAAATAGCCTTTGTAGTTT  
AATAGTAGAACCCATGGAAAACCTGGCTACAGTTGATGTTGAATTGGGACC  
20 CTCAGCAGAGAGGAGGACCTGTTGACCTTACTTTGAAGCAGCCAAGATGT  
TTTGTATTAATGGATCACATTTTGAATTTGAAGATAGTACACATCCTAAA  
TATGACTTCTGCAAAGATAATTTCTTTTCTGTTACCACCTGATGAAAGTC  
TTCATTCACTACAGTCTCGTATTGAGCGTGAACTGGAATAAATACTGGT  
TCTCAAGAACTTCTTTCAGAGACAGGAATTTCTCTGGATCCTCGGAAACC  
25 AGCCTCTCAATGTGTTCTAGATGGAGTTAGAGGCTGTGATAGCTATATGG  
TTTATTTGTTTGATAAAAGTAAACTGTATATGAAGGGCCATTTGCTTCC  
AGAAGTTTATCTGATTGTGTAAATTATATTGTACAGGACAGCAAAATACA  
GCTTCCAATTATACAGCTGCGTAAAGTGTGGGCTGAAGCAGTGCATATG  
TGTCTGGACTAAAAGAAGACTATAGCAGGCTCTTTCAGGGACAAAGGGCA  
30 GCAATGTTAAGTCTTCTTAGATATAATGCTAACTTAACAAAAATGAAGAA  
CACTTTGATCTCAGCATCACAACTGAAAGCTAAATTGGAGTTTTTTC  
ACAAAAGCATTTCAGCTTGACTTGGAGAGATACAGCGAGCAGATGACGTAT  
GGGATATCTTCAGAAAAAATGCTAAAAGCATGGAAAGAAATGGAAGAAAA  
GGCCATCCACTATGCTGAGGTTGGTGTCAATTGGATACCTGGAGGATCAGA  
35 TTATGTCTTTGCATGCTGAAATCATGGAGCTACAGAAGAGCCCCCTATGGA  
AGACGTCAGGGAGACTTGATGGAATCTCTGGAACAGCGTGCCATTGATCT  
ATATAAGCAGTTAAAACACAGACCTTCAGATCACTCCTACAGTGACAGCA  
CAGAGATGGTGAAAATCATTGTGCACACTGTGCAGAGTCAGGACCGTGTG  
CTCAAGGAGCTGTTTGGTCATTTGAGCAAGTTGTTGGGCTGTAAGCAGAA  
40 GATTATTGATCTACTCCCTAAGGTGGAAGTGGCCCTCAGTAATATCAAAG  
AAGCTGACAATACTGTCATGTTTCATGCAGGGAAAAAGGCAGAAAGAAATA  
TGGCATCTCCTTAAAATTGCCTGTACACAGAGTTCTGCCCCGGTCCCTTGT  
AGGATCCAGTCTAGAAGGTGCAGTAACCCCTCAGACATCAGCATGGCTGC  
CCCCGACTTCAGCAGAACATGATCATTCTCTGTGATGTGTGGTAACTCCT  
45 CAAGATGGGGAGACTTCAGCACAAATGATAGAAGAAAATTTGAACTGCCT  
TGGCCATTTAAGCACTATTATTCATGAGGCAAATGAGGAACAGGGCAATA  
GTATGATGAATCTTGATTGGAGTTGGTTAACAGAATGA

SEQ ID NO. 2

IKK $\alpha$ \_3 Targeted Region (mRNA) AAGCAGUGCACUAUGUGUCUG  
Sense siRNA: 5'-GCAGUGCACUAUGUGUCUG*dTdT*-3'  
Antisense siRNA:5'-CAGACACAUAGUGCACUGC*dTdT*-3'

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SEQ ID NO. 3

IKK $\alpha$ \_3 Inverted  
Sense siRNA: 5'-GUCUGUGUAUCACGUGACG*dTdT*-3'  
Antisense siRNA:5'-CGUCACGUGAUACACAG*dTdT*-3'

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SEQ ID NO. 4

IKK $\alpha$ \_1 Targeted Region (mRNA) AACACUGCAGUAUCUGGCCCC  
Sense siRNA: 5'-CACUGCAGUAUCUGGCCCC*dTdT*-3'  
Antisense siRNA:5'-GGGGCCAGAUACUGCAGUG*dTdT*-3'

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SEQ ID NO. 5

IKK $\alpha$ \_2 Targeted Region (mRNA) AAUUGGGACCCUCAGCAGAGA  
Sense siRNA: 5'-UUGGGACCCUCAGCAGAG*dTdT*-3'  
Antisense siRNA:5'-UCUCUGCUGAGGGUCCCA*dTdT*-3'

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SEQ ID NO. 6

IKK $\alpha$ \_4 Targeted Region (mRNA) AAGGCCAUCCACUAUGCUGAG  
Sense siRNA: 5'-GGCCAUCCACUAUGCUGAG*dTdT*-3'  
Antisense siRNA:5'-CUCAGCAUAGUGGAUGGCC*dTdT*-3'

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SEQ ID NO. 7

IKK $\alpha$ \_4 Inverted  
Sense siRNA: 5'- GAGUCGUAUCACCUACCGG*dTdT*-3'  
Antisense siRNA:5'- CCGGUAGGUGAUACGACUC*dTdT*-3'

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SEQ ID NO.8

MERPPGLRPGAGGPWEMRERLGTGGFGNVCLYQHRELDLKIAIKSCRLEL  
STKNRERWCHEIQIMKKLNHANVVKACDVPEELNLIHDPVLLAMEYCSG  
GDLRKLLNKPENCCGLKESQILSLLSDIGSGIRYLHENKIIHRDLKPENI  
35 VLQDVGGKIIHKIIDLGYAKDVDQGSLSCTSFVGTLOYLAPELFENKPYTA  
TVDYWSFGTMVFECIAGYRPFLLHHLQPFTHWEKIKKKDPKCIFACEEMSG  
EVRFSSHLPPQNSLCSLIVEPMENWLQMLNWDPPQRRGGPVDLTLKQPRC  
FVLMDHILNLKIVHILNMTSAKIIISFLLPPDESLHSLQSRIERETGINTG  
SQELLSETGISLDPKRPASQCVLDGVRGCDSYMVYLFDKSKTVYEGPFAS  
40 RSLSDCVNYIVQDSKIQLPITQLRKVWAEAVHYVSGLKEDYSRLFQGGQRA  
AMLSLLRYNANLTKMKNTLISASQQLKAKLEFFHKSIQLDLERYSEQMTY  
GISSEKMLKAWKEMEEKAIHYAEVGVIGYLEDQIMSLHAEIMELQKSPYG  
RRQGDLMESLEQRAIDLKQLKHRPSDHSYSDDSTEMVKIIVHTVQSQDRV  
LKELFGHLSKLLGCKQKIIDLLPKVEVALSNIKEADNTVMFMQGRQKEI  
45 WHLLKIACTQSSARSLVGSSLEGAVTPQTSAWLPPTSAEHDHSLSCVVTP  
QDGETSAQMIEENLNCLGHLSTIIHEANEEQGNMMLDWSWLTE

Case 9/263 US

SEQ. ID. No. 9

Forward primer 5'-GCACAGAGATGGTGAAAATCATTG-3'

5 SEQ. ID. No. 10

Reverse primer 5'-CAACTTGCTCAAATGACCAAACAG-3'.

SEQ. ID. No. 11

The probe sequence 5'-TGAGCACACGGTCCTGACTCTGCA